REMARKS

The present amendment was made to correct the multiple dependencies and to further clarify the invention. Support for new claims 433-444 can be found in the application as originally filed. See the specification, for instance, at page 77 (whole page) to page 79, line 10. Claims 1-22 and 433-444 are pending in this case. No new matter has been added to the application as a result of the present amendment.

Prompt consideration and entry of this amendment prior to examination is respectfully requested. The Commissioner is authorized to deduct any fees associated with this amendment from Deposit Account No. 13-2490.

Respectfully submitted,

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APPENDIX
(clean copy of pending claims)

1. A method of detecting a nucleic acid having at least two portions comprising:

providing a type of nanoparticles having oligonucleotides attached thereto, the oligonucleotides on each nanoparticle having a sequence complementary to the sequence of at least two portions of the nucleic acid;

contacting the nucleic acid and the nanoparticles under conditions effective to allow hybridization of the oligonucleotides on the nanoparticles with the two or more portions of the nucleic acid; and

observing a detectable change brought about by hybridization of the oligonucleotides on the nanoparticles with the nucleic acid.

2. A method of detecting nucleic acid having at least two portions comprising:

contacting the nucleic acid with at least two types of nanoparticles having oligonucleotides attached thereto, the oligonucleotides on the first type of nanoparticles having a sequence complementary to a first portion of the sequence of the nucleic acid, the oligonucleotides on the second type of nanoparticles having a sequence complementary to a second portion of the sequence of the nucleic acid, the contacting taking place under conditions effective to allow hybridization of the oligonucleotides on the nanoparticles with the nucleic acid; and

observing a detectable change brought about by hybridization of the oligonucleotides on the nanoparticles with the nucleic acid.

3. The method of Claim 2 wherein the contacting conditions include freezing and thawing.

4. The method of Claim 2 wherein the contacting conditions include heating.

5. The method of Claim 2 wherein the detectable change is observed on a solid surface.

6. The method of Claim 2 wherein the detectable change is a color change observable with the naked eye.

7. The method of Claim 6 wherein the color change is observed on a solid surface.

8. The method of Claim 2 wherein the nanoparticles are made of gold.

9. The method of Claim 2 wherein the oligonucleotides attached to the nanoparticles are labeled on their ends not attached to the nanoparticles with molecules that produce a detectable change upon hybridization of the oligonucleotides on the nanoparticles with the nucleic acid.

10. The method of Claim 9 wherein the nanoparticles are metallic or semiconductor nanoparticles and the oligonucleotides attached to the nanoparticles are labeled with fluorescent molecules.

11. The method of Claim 2 wherein:

the nucleic acid has a third portion located between the first and second portions, and the sequences of the oligonucleotides on the nanoparticles do not include sequences complementary to this third portion of the nucleic acid; and

the nucleic acid is further contacted with a filler oligonucleotide having a sequence complementary to this third portion of the nucleic acid, the contacting taking place under conditions effective to allow hybridization of the filler oligonucleotide with the nucleic acid.

12. The method of Claim 2 wherein the nucleic acid is viral RNA or DNA.

13. The method of Claim 2 wherein the nucleic acid is a gene associated with a disease.

14. The method of Claim 2 wherein the nucleic acid is a bacterial DNA.

15. The method of Claim 2 wherein the nucleic acid is a fungal DNA.

16. The method of Claim 2 wherein the nucleic acid is a synthetic DNA, a synthetic RNA, a structurally-modified natural or synthetic RNA, or a structurally-modified natural or synthetic DNA.

17. The method of Claim 2 wherein the nucleic acid is from a biological source.

18. The method of Claim 2 wherein the nucleic acid is a product of a polymerase chain reaction amplification.

19. The method of Claim 2 wherein the nucleic acid is contacted with the first and second types of nanoparticles simultaneously.

20. The method of Claim 2 wherein the nucleic acid is contacted and hybridized with the oligonucleotides on the first type of nanoparticles before being contacted with the second type of nanoparticles.

21. The method of Claim 20 wherein the first type of nanoparticles is attached to a substrate.

22. The method of Claim 2 wherein the nucleic acid is double-stranded and hybridization with the oligonucleotides on the nanoparticles results in the production of a triple-stranded complex.

433. The method according to any one of claims 1 or 2, wherein the oligonucleotides are attached to the nanoparticles in a stepwise ageing process comprising (i) contacting the oligonucleotides with the nanoparticles in a first aqueous solution for a period of time sufficient to allow some of the oligonucleotides to bind to the nanoparticles; (ii) adding at least one salt to

the aqueous solution to create a second aqueous solution; and (iii) contacting the oligonucleotides and nanoparticles in the second aqueous solution for an additional period of time to enable additional oligonucleotides to bind to the nanoparticles.

434. The method according to claim 433, wherein the salt solution has an ionic strength sufficient to overcome at least partially the electrostatic attraction or repulsion of the oligonucleotides for the nanoparticles and the electrostatic repulsion of the oligonucleotides for each other.

435. The method of Claim 433 wherein the nanoparticles are metal nanoparticles or semiconductor nanoparticles.

436. The method of Claim 435 wherein the nanoparticles are gold nanoparticles.

437. The method of Claim 436 wherein the oligonucleotides include a moiety comprising a functional group which can bind to a nanoparticle.

438. The method of Claim 433 wherein all of the salt is added to the water in a single addition.

439. The method of Claim 433 wherein the salt is added gradually over time.

440. The method of Claim 433 wherein the salt is selected from the group consisting of sodium chloride, magnesium chloride, potassium chloride, ammonium chloride, sodium acetate, ammonium acetate, a combination of two or more of these salts, one of these salts in a phosphate buffer, and a combination of two or more these salts in a phosphate buffer.

441. The method of Claim 440 wherein the salt is sodium chloride in a phosphate buffer.

442. The method of Claims 1 or 2 wherein the oligonucleotides present on surface of the nanoparticles at a surface density of at least 10 picomoles/cm^2.

443. The method of Claim 442 wherein the oligonucleotides are present on surface of the nanoparticles at a surface density of at least 15 picomoles/cm^2.

444. The method of Claim 443 wherein the oligonucleotides are present on surface of the nanoparticles at a surface density of from about 15 picomoles/cm^2 to about 40 picomoles/cm^2.